REMARKS

Claims 89-102, 104-106, 108, 124, 125, 127-130, 132-135, 137-147, and 149-164 remain pending after response.

Interview with Examiner

This will acknowledge the recent telephone interview with the Examiner during which the undersigned informed the Examiner that executed Declarations under 37 CFR 1.132 were being submitted by way of supplemental response to the previous response. The Examiner kindly indicated that he would defer examination of applicant's prior response pending receipt of the attached Declarations if submitted by June 27, 2008. The undersigned thanks the Examiner for his cooperation in this matter.

Rejection under 35 USC 103(a)

Claims 89-96, 98, 99, 101, 102, 104-106, 108, 124, 125, 127-130, 132-135, 139-147, 149 and 152-164 stand rejected under 35 USC 103(a) as being unpatentable over *Jackson* in view of *Riley et al*, *Klampfer et al*, *Wawretschek et al*, *Herschler '421*, *Herschler '039* and *Menon et al.* This rejection is respectfully traversed.

The claimed method is neither disclosed nor suggested by the cited prior art, as is apparent from the previous discussion of the deficiencies of the prior art relied upon by the Examiner (see response of March 24, 2008).

By way of review, the claims as presently on file are all directed to a method of treating neoplastic disease in a human or animal patient comprising administering to the patient an anti-neoplastic effective amount of a composition comprising:

(a) ***a physiologically acceptable source of assimilable copper***;

(b) ***salicylic acid or an alkali or alkaline earth metal salt thereof***;

(c) ***vitamin C***; and

(d) ***a physiologically acceptable source of assimilable manganese***.

These claims are based on the inventor's surprising discovery that a composition containing at least these four components (and optionally, but not necessarily, others) is effective in combating neoplastic disease.

The applicant again maintains that the presently claimed methods are neither disclosed nor suggested by said art, for the following reasons.

Applicant will not repeat in detail in this Supplemental Response those distinctions that exist between the claimed invention and the cited prior art, but directs the Examiner's attention to such distinctions that are discussed at length in applicant's response of March 24, 2008.

Given such deficiencies in the prior art relied upon by the Examiner, a *prima facie* case of obviousness has not been established by the Examiner.

By way of summary of the distinctions between the claimed invention and the cited prior art, applicant states as follows:

- The cited prior art teaches that vitamin and mineral supplements can be used to improve general health (which may have a knock on effect in reducing the risk of contracting diseases in general);
- The cited prior art teaches that aspirin (or similar acetylated salicylates), if added to vitamin supplements, may be beneficial in terms of general health and reducing the risk of contracting disease;

- The cited prior art teaches that sodium salicylate has, on its own or in combination with the removal of growth factor or addition of daunorubicin, been shown to be effective *in-vitro* as in inducing apoptosis in certain cell lines and, for that reason, it has been proposed that sodium salicylate *may* have therapeutic *potential* as an anti-cancer agent;
- The cited prior art teaches that sodium salicylate is a general analgesic whose analgesic effect can be improved by addition of orotic acid or a tolerable orotate salt;
- The cited prior art teaches that MSM *may* have some efficacy in treating neoplastic disease; and
- The cited prior art teaches that vitamin C has been shown to be effective in-vitro in reducing cell viability in certain cell lines, and has for that reason been suggested as an anti-cancer agent for cancer cells.

The above teachings, taken alone or together, fall far short of disclosing, suggesting, or rendering obvious, the claimed method.

Indeed, much of the art relied upon by the Examiner *does not even refer to cancer treatment*, while such art which *does* refer to cancer treatment refers only to the possible use of certain compounds singly and in isolation (or else in combination with compounds other than those claimed).

There is no teaching in the art as a whole regarding a *combination of* manganese, copper, vitamin C and sodium salicylate (or salicylic acid or other alkali or alkaline earth metal salts thereof) as a treatment for cancer, nor is there any obvious reason why one of ordinary skill in the art, on reading the cited documents (not to mention the multitude of other prior art documents

relating to possible cancer treatments) would decide to investigate or adopt such a combination as a treatment for cancer.

In particular, the cited art provides no indication or suggestion of the additive benefits of the claimed combination of components in treating cancer, or of the resulting efficacy of the combination as a cancer treatment, absent which the claimed combination is but one of hundreds (if not thousands) of combinations which merely could be investigated for such purpose.

There are many putative and established anti-cancer agents available, but that does not make the combination of any and all such asserted agents obvious. There is no reason to consider, in advance, that two different anti-cancer compounds operating (according to Klamfer and Memnon) in different manners (as regards their biochemical targets) will have beneficial effects if combined – as is illustrated by Klamfer itself, which considers the synergistic effects of sodium salicylate and another known anti cancer agent (daunorubicin) surprising. Indeed, it is just as possible that two anti-cancer agents could provide no additive effect, or that the two agents could have conflicting effects (thus reducing overall efficacy).

Likewise, there is even less reason to consider that adding a compound having *no known anti-cancer effect* would be beneficial, whereas adding such additional compounds could still have adverse effects on the efficacy of the composition, or other unforeseen and undesired side effects. Thus where, as in the present case, the cited art provides no teaching to suggest to one of ordinary skill in the art that a claimed combination of compounds could or should beneficially be used in combined in a claimed method of therapy, it is submitted that the claimed subject matter is not obvious.

It is respectfully submitted, based on the above distinctions and those arguments previously presented, that the prior art not only fails to suggest the claimed invention, but it

would not have been within the ability of one of ordinary skill in the art to arrive at the claimed invention, nor would one of ordinary skilled in the art have been motivated to modify the prior art in the manner asserted by the Examiner to arrive at the method as claimed.

Much of the prior art relied on by the Examiner does not relate to treating neoplastic disease, and it would not have been obvious to one of ordinary skill in the art to refer to such documents at all, nor would one of ordinary skill have obtained any useful information therefrom regarding cancer treatment had he or she done so. Conversely, the art which does refer to cancer treatment is directed only to the possible potential use of certain of the claimed compounds in isolation (or in combination with compounds other than those claimed), and provides no teaching that would have lead one of ordinary skill in the art to the presently claimed combination as a treatment for cancer.

It is not applicant's contention that the claimed invention is non-obvious because the claimed combination of active ingredients employed in the claimed method is not disclosed in a single reference, but rather that the claimed invention is not rendered obvious from the art as a whole. Applicant recognizes there is no requirement that all of the components have an anti-neoplastic effect so long as the composition used in the claimed method has the desired anti-neoplastic effect. The relevant question, however, is *whether it would have been obvious to one of ordinary skill in the art to administer the combined combination of components in an anti-neoplastic treatment.*

As explained above, it would not have been obvious from the art cited that even the combination of ascorbic acid and sodium salicylate (suggested individually in Klamfer and Memnon as compounds having possible utility as anti-cancer agents) would be beneficial (as compared to their use individually), let alone that other compounds having no indicated anti-

neoplastic effects (copper and manganese) could or should additionally be combined with advantage.

The fact that copper and manganese are used in multinutrient compositions does not make it obvious to add them to an anti-cancer composition (or else multinutrients would be commonly added to all anti-cancer compositions, which is clearly not the case).

No *prima facie* case of obviousness has accordingly been presented, and the rejection under 35 USC 103(a) is improper and should be withdrawn.

Despite the fact that no *prima facie* case of obviousness has been presented by the Examiner, applicant nonetheless provides evidence demonstrating the enhanced effects in treating cancer of the claimed combination of compounds, as compared to the components individually. Such enhanced effects of the claimed combination are not obvious from the cited art nor, for the reasons set out above, would it have been "well within the skill of one of ordinary skill in the art" to arrive at the presently claimed combination of components in the expectation that the resulting combination would be effective as anti-neoplastic composition.

The data provided in the application (cf. Examples 11 to 18) clearly demonstrates the striking effects of compositions comprising said four components in treating cancer. In each of said studies, the compositions in accordance with the invention (consisting of sodium salicylate, vitamin C, manganese orotate, and copper gluconate or orotate) were effective in inhibiting, halting, or even reversing tumour growth. Reference is made, in particular to Examples 11 and 13 and related Tables 1 and 2 of the application, in which studies the mice treated with the claimed compositions had significant reductions in tumour mass and increases in life expectancy as compared to the control mice.

As further evidence of the efficacy of the claimed compositions in treating neoplastic disease, applicant submits herewith two Declarations under 37 CFR 1.132 verifying the substance of reports of two further animal studies investigating the anti-neoplastic effects of a composition within the scope of the claimed invention (referred to as CV247) consisting of sodium salicylate, vitamin C, manganese gluconate, and copper gluconate (which studies were previously discussed in applicant's response of March 24, 2008).

This data demonstrates that animals treated with the compositions of the present invention show a clear reduction in tumour mass/volume as compared to the control animals untreated with the compositions. Moreover, this data also supports the teaching of the present application that it is the claimed combination of components that leads to the particular efficacy of the claimed compositions in treating cancer. In particular, the compositions comprising all the claimed components (CV247) had demonstrably greater benefits than sodium salicylate alone, or in combination with vitamin C. Applicant directs the Examiner's attention to the substance of the two attached Declarations during his review of this response.

It is believed that such comparative data clearly demonstrates the efficacy of the claimed invention, as well as the enhanced effect of the combination of the recited components in the treatment of cancer.

The undersigned acknowledges the Interview Summary Record issued by the Examiner directed to the substance of an interview of May 9, 2008 during which the substance of the attached Declarations was discussed. It is noted that the Interview Summary Record states that the attached data, "if verified, that the data would move prosecution forward provided that claims are amended to claim the gluconate or orotate salt with respect to the minerals."

While applicant is appreciative for the Examiner's comments, applicant disagrees with the premise of the Examiner that only claims of such limited scope should be found allowable. Indeed, absent the presentation of a *prima facie* case of obviousness, which the Examiner has not done, it is not appropriate for the Examiner to restrict the scope of the claims based on the presentation of such comparative data to gluconate or orotate salts (the presentation of which is not required to overcome a rejection which does not present a *prima facie* case of obviousness).

Even if, *arguendo*, a *prima facie* case of obviousness is believed to have been presented, the present record is nonetheless supportive of the allowance of broad claims, and not claims of a scope limited as proposed by the Examiner. The Examiner provides no reason why claims directed to a multitude of salts (as disclosed) would be not be allowable, as opposed to claims limited to only gluconate and orotate salts.

The rejection under 35 USC 103(a) is this without basis and should be withdrawn. All claims under rejection should be allowed.

The application is now in condition for allowance. Allowance of claims directed to the generic invention is believed proper.

Respectfully submitted,

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Attachments: Two executed Declarations under 37 CFR 1.132 of Roger Anthony Oakes